TS

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
RE/P45122		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/EP 98/ 07521	16/11/1998	19/11/1997
Applicant		
SMITHKLINE BEECHAM BIOLOGICALS S.A. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   [X] contained in the international application in written form.

   [ ] filed together with the international application in computer readable form.

   [ ] furnished subsequently to this Authority in written form.

   [X] furnished subsequently to this Authority in computer readble form.

   [X] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [X] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

   [ ] the text is approved as submitted by the applicant.

   [X] the text has been established by this Authority to read as follows:

   RECOMBINANT ALLERGEN WITH REDUCED ENZYMATIC ACTIVITY

5. With regard to the **abstract,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. _____

   [ ] as suggested by the applicant.

   [ ] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

   [X] None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 98/ 07521

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Remark: Although claim 22
is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the vaccine.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

[redacted]ational Application No
[redacted]/EP 98/07521

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/12 C12N15/57 C07K14/435 A61K39/35

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C12N C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	TOPHAM CM ET AL: "Comparative modelling of major house dust mite allergen Der pI: structure validation using an extended environmental amino acid propensy table" PROTEIN ENGINEERING., vol. 7, no. 7, 1994, pages 869-894, XP002101656 ENGLAND GB cited in the application see page 869, right-hand column, last paragraph ---	1-4,18, 21,22
X	WO 94 05790 A (IMMULOGIC PHARMACEUTICAL CORPORATION ;THOMAS WR (AU); CHUA K-Y (AU)) 17 March 1994 see page 47 - page 49; examples 1-4 --- -/--	11

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
6 May 1999	18/05/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Cupido, M

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Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	HEWITT CR ET AL: "Heterogeneous proteolytic specificity and activity of the house dust mite proteinase allergen Der p I." CLINICAL AND EXPERIMENTAL ALLERGY, , vol. 27, no. 2, February 1997, pages 201-207, XP002101657 ENGLAND see page 206, left-hand column ---	1-22
A	HEWITT CR ET AL: "A major house dust mite allergen disrupts the immunoglobulin E network by selectively cleaving CD23: innate protection by antiproteases." JOURNAL OF EXPERIMENTAL MEDECINE, vol. 182, no. 5, November 1995, pages 1537-1544, XP002101668 UNITED STATES -----	1-22

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/EP 98/07521

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9405790 A	17-03-1994	US 5433948 A	18-07-1995
		AT 163674 T	15-03-1998
		AU 680202 B	24-07-1997
		AU 4854893 A	29-03-1994
		CA 2144055 A	17-03-1994
		DE 69317292 D	09-04-1998
		DE 69317292 T	18-06-1998
		DK 662129 T	30-03-1998
		EP 0662129 A	12-07-1995
		ES 2112996 T	16-04-1998
		GR 3026711 T	31-07-1998
		JP 8504179 T	07-05-1996
		NZ 256255 A	29-03-1999
		US 5773002 A	30-06-1998
		US 5770202 A	23-06-1998
		US 5552142 A	03-09-1996

ATENT COOPERATION TR. TY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

United States Patent and Trademark Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 18 June 1999 (18.06.99)	
International application No. PCT/EP98/07521	**Applicant's or agent's file reference** RE/P45122
International filing date (day/month/year) 16 November 1998 (16.11.98)	**Priority date** (day/month/year) 19 November 1997 (19.11.97)
Applicant BRUCK, Claudine et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

17 April 1999 (17.04.99)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Jean-Marie McAdams

Telephone No.: (41-22) 338.83.38

PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : C12N 15/12, C07K 14/435, A61K 39/35 — A2

(11) International Publication Number: WO 99/25823

(43) International Publication Date: 27 May 1999 (27.05.99)

(21) International Application Number: PCT/EP98/07521

(22) International Filing Date: 16 November 1998 (16.11.98)

(30) Priority Data:
9724531.0 19 November 1997 (19.11.97) GB

(71) Applicant *(for all designated States except US)*: SMITHKLINE BEECHAM BIOLOGICALS S.A. [BE/BE]; Rue de l'Institut 89, B–1330 Rixensart (BE).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: BRUCK, Claudine [BE/BE]; SmithKline Beecham Biologicals S.A., Rue de l'Institut 89, B–1330 Rixensart (BE). BOLLEN, Alex [BE/BE]; Université Libre de Bruxelles, Service de Génétique Appliquée, Rue de l'Industrie 24, B–1400 Nivelles (BE). JACOBS, Paul [BE/BE]; Université Libre de Bruxelles, Service de Génétique Appliquée, Rue de l'Industrie 24, B–1400 Nivelles (BE). MASSAER, Marc [BE/BE]; Université Libre de Bruxelles, Service de Génétique Appliquée, Rue de l'Industrie 24, B–1400 Nivelles (BE).

(74) Agent: DALTON, Marcus, Jonathan, William; SmithKline Beecham plc, Corporate Intellectual Property, Two New Horizons Court, Brentford, Middlesex TW8 9EP (GB).

(81) Designated States: CA, JP, US, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published
Without international search report and to be republished upon receipt of that report.

(54) Title: RECOMBINANT ALLERGEN WITH REDUCED ENZYMATIC ACTIVITY

(57) Abstract

The present invention provides a novel treatment for allergy comprising the provision of a recombinant allergen with reduced enzymatic activity. Vaccines comprising said mutant allergens stimulate a Th1–type immune response in allergic or naïve individuals, thereby reducing the potential for an allergic response upon contact with wild–type allergen. Preferably said allergen is DerP1.

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WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 :
C12N.15/12, 15/57, C07K 14/435, A61K 39/35

A3

(11) International Publication Number: WO 99/25823

(43) International Publication Date: 27 May 1999 (27.05.99)

(21) International Application Number: PCT/EP98/07521

(22) International Filing Date: 16 November 1998 (16.11.98)

(30) Priority Data:
9724531.0 19 November 1997 (19.11.97) GB

(71) Applicant *(for all designated States except US)*: SMITHKLINE BEECHAM BIOLOGICALS S.A. [BE/BE]; Rue de l'Institut 89, B–1330 Rixensart (BE).

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(75) Inventors/Applicants *(for US only)*: BRUCK, Claudine [BE/BE]; SmithKline Beecham Biologicals S.A., Rue de l'Institut 89, B–1330 Rixensart (BE). BOLLEN, Alex [BE/BE]; Université Libre de Bruxelles, Service de Génétique Appliquée, Rue de l'Industrie 24, B–1400 Nivelles (BE). JACOBS, Paul [BE/BE]; Université Libre de Bruxelles, Service de Génétique Appliquée, Rue de l'Industrie 24, B–1400 Nivelles (BE). MASSAER, Marc [BE/BE]; Université Libre de Bruxelles, Service de Génétique Appliquée, Rue de l'Industrie 24, B–1400 Nivelles (BE).

(74) Agent: DALTON, Marcus, Jonathan, William; SmithKline Beecham plc, Corporate Intellectual Property, Two New Horizons Court, Brentford, Middlesex TW8 9EP (GB).

(81) Designated States: CA, JP, US, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(88) Date of publication of the international search report:
15 July 1999 (15.07.99)

(54) Title: RECOMBINANT ALLERGEN WITH REDUCED ENZYMATIC ACTIVITY

(57) Abstract

The present invention provides a novel treatment for allergy comprising the provision of a recombinant allergen with reduced enzymatic activity. Vaccines comprising said mutant allergens stimulate a Th1–type immune response in allergic or naïve individuals, thereby reducing the potential for an allergic response upon contact with wild–type allergen. Preferably said allergen is DerP1.

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DK	Denmark	**LK**	Sri Lanka	**SE**	Sweden		
EE	Estonia	**LR**	Liberia	**SG**	Singapore		

Claims

1. A recombinant mutant allergen wherein said mutant allergen has reduced enzymatic activity compared to the wild-type allergen.

2. A recombinant mutant allergen as claimed in claim 1, wherein said allergen is based upon a type I cysteine protease allergen.

3. A recombinant mutant allergen as claimed in claim 1, wherein said allergen is based upon DerP1 from *Dermatophagoides pteronyssinus*.

4. A recombinant mutant allergen as claimed in claim 3, wherein said mutant DerP1 comprises an active site mutant.

5. A recombinant mutant allergen as claimed in claim 4, wherein said active site mutant DerP1 comprises a mutation of the Cys 34 residue.

6. A recombinant mutant allergen as claimed in claim 5, wherein said mutation of the Cys 34 residue comprises an alanine substitution.

7. A recombinant mutant allergen as claimed in claim 4, wherein said active site mutant DerP1 comprises a mutation of the His 170 residue.

8. A recombinant mutant allergen as claimed in claim 3, wherein said mutant DerP1 comprises a mutation at the site of cleavage between the propeptide and the mature molecule.

9. A recombinant mutant allergen as claimed in claim 8, wherein said mutation at the site of cleavage between the propeptide and the mature molecule comprises a deletion of the residues NAET.

10. A recombinant mutant allergen as claimed in claim 3, wherein said mutation comprises the deletion or substitution of cysteine residues which are involved in disulphide bridge formation.

11. Stable recombinant DerP1.

12. A recombinant mutant allergen having the sequence as set out in SEQ ID NO. 1

13. A recombinant mutant allergen having the sequence as set out in SEQ ID NO. 2

14. A recombinant mutant allergen having the sequence as set out in SEQ ID NO. 3

15. A recombinant mutant allergen having the sequence as set out in SEQ ID NO. 4

16. A recombinant mutant allergen having the sequence as set out in SEQ ID NO. 5

17. An isolated nucleic acid molecule encoding a mutated version of an allergen as claimed in any one of claims 1 to 16.

18. A vaccine comprising a recombinant mutant allergen as claimed in any one of claims 1 to 17, and an adjuvant.

19. A vaccine as claimed in claim 18, wherein the adjuvant is a preferential stimulator of Th1-type immune responses.

20. A vaccine as claimed in claim 18, wherein the adjuvant comprises one or both of QS21 and 3-O-deacylated monophosphoryl lipid A.

21. Use of a recombinant mutant allergen in the manufacture of a medicament for the treatment of allergy.

22. A method of treating or preventing allergic responses comprising administering to an individual suffering from or susceptible to allergy a vaccine as claimed in claim 18.

4

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
RE/DM/B45122		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP98/07521	16/11/1998	19/11/1997
International Patent Classification (IPC) or national classification and IPC C12N15/12		
Applicant SMITHKLINE BEECHAM BIOLOGICALS S.A. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
17/04/1999	20. 01. 00
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Roscoe, R Telephone No. +49 89 2399 2554

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP98/07521

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-25	as originally filed				

Claims, No.:

1-22	as received on	10/11/1999	with letter of	08/11/1999	

Drawings, sheets:

1/9-9/9	as originally filed

2. The amendments have resulted in the cancellation of:

☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims 2-17
	No:	Claims 1, 18-22
Inventive step (IS)	Yes:	Claims
	No:	Claims 1-22
Industrial applicability (IA)	Yes:	Claims 1-21
	No:	Claims 22

2. Citations and explanations

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

1. Citations

The documents mentioned in the present International Preliminary Examination Report are numbered as in the search report, i.e. D1 corresponds to the first document of the search report etc.

2. Reasoned statement on Novelty, Inventive Step and Industrial Applicability (Section V)

2.1 Novelty (Art.33(2) PCT)

Due to the lack of specificity of the term allergen (see section 3.1) and the fact that hundreds of mutants of proteins with reduced enzymatic activity are known which could be allergens, novelty cannot be acknowledged for claim 1. Due to the widespread use of recombinant proteins in vaccines, novelty can also not be acknowledged for claims 18-22.

2.2 Inventive Step (Art.33(3) PCT)

The amino acid sequence of proDerP1 and even of preproDerP1 is known in the art (e.g. D2, Fig.21, bottom p.17).

The prior art (e.g. D3 and D4) clearly states that there is a connection between DerPI protease activity and allergenicity. D2 (top p.21) suggests using fragments (which can be considered as deletion mutants) of DerPI for therapy where molecules of limited allergenicity may increase safety of desensitization. It is thus logical to seek fragments or derivatives which lack protease activity. D1 identifies the Cys34 and His170 residues, which are applicants preferred mutants, as critical components of the active site of DerP1 (p.890, 2nd para.) and thus even enables a highly specific approach to knockout of the enzyme activity. Hence, given that the necessary technical information was available to the skilled person and also that he would have been motivated to provide protease-negative DerPI, the present application is not considered to comprise any inventive subject-matter. Argumentation that D2 refers to small peptide fragments is in itself correct, yet clearly the advantage of the small fragments is the reduced allergenicity (the clear

disadvantage is that not all relevant epitopes are found on a given fragment). Given that the link between allergenicity and enzymatic activity was explained (in D4) after D2, a skilled person knowing the content of D2 and subsequently being presented with another method of reducing allergenicity would clearly be inclined to use this method. Indeed D2 states on p.13, l.18-28 that the amino acid sequence may be altered to reduce allergenicity (thus improving therapeutic qualities). The same paragraph cleary states that the "peptide" includes the entire Derpl sequence. This leaves the skilled person merely waiting for knowledge of how exactly to do this - this knowledge is presented in D1 and D4.

2.3 **Industrial Applicability (Art.33(4) PCT)**

For the assessment of the present claim 22 on the question whether it is industrially applicable, no unified criteria exist in the PCT. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

3. **Certain observations (Section VIII)**

3.1 **Clarity (Art.6 PCT)**

The term "allergen" cannot be accepted to rule out any proteins with antigenic properties from the scope of a claim. All antigens are potential allergens. Different test animals cannot be expected to react uniformly to antigens (some may experience an allergic response, others not). Given that no uniform system is available to determine if a compound is an allergen or not, said term cannot be used to define any specific characteristics of a product. The publication by Platt-Mills in the supplement to the Journal of Allergy and Clinical Immunology (Vol.100, No.6, Part 1 (1997)) does not prove that the term "allergen" has a defined meaning. The article merely states how an allergen can receive WHO/IUIS nomenclature (p.S8, col.1). Indeed this suggests that only a subgroup of allergens receives the nomenclature, whereas others exist. Applicant does not

appear to have referred to this nomenclature system in the application documents. Indeed, there appear to be multiple sources of standards in the field of allergen research (p.S5, col.1, "Some allergen standards..."). Thus applicant will need to introduce further technical features into claim 1 to render it acceptable with respect to novelty.

The terminology "substantially full length" which has been introduced into claim 1 cannot be considered as a clear technical feature since the term "substantial" does not define any particular size in a uniformly recognized manner. Hence, this feature shall not be considered as limiting.

The term "stable" in claim 11 has to be considered technically meaningless. A parameter indicating how stable the DerPI is, and the technical features causing this increased stability need to be introduced into the claim. The fact that the description mentions what is meant by the term stable does not mean that the explanation of the term can be omitted from the claim in question. Further, the stability-related statement on p.4 of the description refers to DerP1 and not pro-DerP1. Additionally, claim 11 is not allowable as it is a claim to a result to be achieved. The method by which the result is achieved (reduction of enzymatic activity) which forms the basis for the present application and is thus an essential feature is not mentioned. Indeed it is not even clear whether the proDerP1 protein is enzymatically active in the first place.

Claim 11 does not refer to a recombinant mutant allergen having reduced enzymatic activity (note: thus also extending beyond scope of invention). Thus inclusion of reference to said claim in claim 18 is inappropriate.